Form 3

# Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2020)

Date：2021/03/31

To Director of Institute for Molecular and Cellular Regulation, Gunma University

| Principal Applicant | |
|---|---|
| Institution | Kyushu University |
| Position | Associate Professor |
| Name | Ka Fai William TSE |

We report on the results of joint research in fiscal 2020 as below.

（Program No. 18003 ）

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| 1． Research Title | Triclosan: a risk factor of fatty liver disease |
| 2． Purpose and Significance of the research project | The project aims to understand the developmental toxicity of a common environmental pollutant, triclosan (TCS), on its stimulatory effects on developing the fatty liver disease. TCS and its degradation by-product, 2,4-Dichlorophenol (2,4-DP), can be found in the environment worldwide. Their potential toxicities on the lipid metabolism and liver development are not well known. We hypothesize that the exposure of TCS and 2,4-DP will promote the development of fatty liver. The transgenic zebrafish model will be used to perform functional assays; together with the next generation sequencing, the potential link between the TCS and fatty liver will be uncovered. |
| 3． Period of The Program | April 1, 2020 ～ March 31, 2021 |

4． Project Members

| Name | Age | Gender | Institution/Department | Position | Role |
|---|---|---|---|---|---|
| (Principal Applicant) Ka Fai William TSE | 37 | M | Kyushu University, Faculty of Agriculture | Associate Professor | Project director |
| (Research Collaborators) Yun-jin JIANG | 56 | M | National Health Research Institutes, Institute of Molecular and Genomic Medicine | Associate Investigator | Expert in zebrafish genetics / Advisor |
| Keng Po LAI | 44 | M | Guilin Medical University, Guangxi Key Laboratory of Tumor Immunology and Microenvironmental Regulation | Professor | Expert in RNA-sequencing and bioinformatics/ Advisor |
| May-su YOU | 57 | F | National Health Research Institutes, Institute of Molecular and Genomic Medicine | Senior Specialist | Expert in zebrafish genetics / Advisor |

※If additional space is required, attach a separate sheet.

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|---|---|---|---|---|
| 5． Collaborative Researcher of IMCR | Name of the Laboratory | Integrated Signaling Systems | Name | Tohru ISHITANI |

6. Research Plans

The drastic advancement in industrialization and technology and the growth in human population in the past century have resulted in unprecedented environmental changes in human history. The production of large amounts of synthetic chemicals and pollutants has influenced our ecosystem and brings potential hazards to humans. The project aims to identify the general toxicity of an endocrine disrupting chemical, triclosan (TCS) and its degradation by-product 2,4-dichlorophenol (2,4-DP) by using the zebrafish model. Zebrafish has been widely used in the developmental studies as an excellent *in vivo*, high-throughput and scalable system for decades. The fatty liver mutant (*trappc11*$^{-/-}$) induced ER stress and altered the protein trafficking that resulting in hepatic steatosis. Here, we would like to investigate if the TCS and 2,4-DP could stimulate the disease development. The project will uncover the underlying mechanism by various biological functional assays, next-generation sequencing, and bioinformatics analysis.

7. Research results:

In the past years, we have identified the general toxicity of TCS and its degradation by-product 2,4-DP in the wild-type and liver- GFP labeled zebrafish. In addition, we have applied the fatty liver mutant line to perform the general characterization of metabolic genes and enzymes under the acute TCS and 2,4-DP exposure. Results suggested that the TCS and 2,4-DP could influence the lipid metabolism during early embryogenesis. In the past year, we plan to prepare samples for the next generation sequencing to dissect the genetic information of the TCS/ 2,4-DP exposed embryos. However, due to the outbreak of the COVID-19, the experimental progress has been heavily interrupted. Currently, our experimental work is getting back to normal, and we will keep on working on the remaining sequencing experiment to fully understand the potential link between the TCS/ 2,4-DP and fatty liver. Lastly, we have published two review articles that describe the usage of zebrafish in cancer and toxicological study; and one research article on the facial development (refer to section 8.2). And we are preparing a manuscript for the first part of the developmental toxicity results in this project.

8. Publications and/or Presentations resulting from Joint Research Program with IMCR.
Exchange of information on joint research with faculty members.

①Please describe a list of publications in which the name of the collaborative researcher of IMCR appears and send one paper reprints of each publication to IMCR.

N/A

②Please describe a list of publications which include the description that the research is supported by Joint Research Program with IMCR and send one copy of each publication to IMCR.

1) KP. Lai, J. Chen, **WKF. Tse**. Role of deubiquitinases in human cancers: Potential targeted therapy. 2020. *International Journal of Molecular Sciences*. 21: 2548.

2) R. Li, C. Huang, JCH. Ho, CCT. Leung, RYC. Kong, Y. Li, X. Liang, KP. Lai, **WKF. Tse**. The use of glutathione to reduce oxidative stress status and its potential for modifying the extracellular martix organization in cleft lip. 2021. *Free Radical Biology and Medicine*. 164: 130-138.

3) KP. Lai, Z. Gong, **WKF. Tse**. Zebrafish as the toxicant screening model: Transgenic and omics approaches. 2021. *Aquatic Toxicology*. 234: 105813.

③Enter the name of the conference, the date of the conference, and the title of the presentation of the conference.(up to 3 cases)

N/A

④Implementation status of information exchange with faculty members in charge of joint research.

We keep regular communication through email.